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INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 7 : A23L 1/30, 1/03 | A61K 31/194, 31/365, A23L | A1

(11) International Publication Number: WO 00/15051

(43) International Publication Date: 23 March 2000 (23.03.00)

(21) International Application Number: PCT/US99/21099

(22) International Filing Date: 14 September 1999 (14.09.99)

(30) Priority Data: 09/151,806 14 September 1998 (14.09.98) US

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(81) Designated States: CA, IN, JP, European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).

Published
With international search report.
Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.

(54) Title: HYDROXYCITRIC ACID COMPOSITIONS

(57) Abstract

Disclosed is a hydroxycitric acid composition and method for preparing it, which comprises partial calcium salts of hydroxycitric acid, and which is essentially potassium–free and prepared from an extract of the *Garcinia sp* fruit. The composition is highly water solube, has minimal hygroscopicity, and has favorable flavor and aesthetic properties.

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HYDROXYCITRIC ACID COMPOSITIONS

FIELD OF THE INVENTION

This invention is directed to hydroxycitric acid ("HCA") compositions, specifically to compositions comprising partial calcium salts of HCA, dietary supplements and food products containing such compositions, and the use of such compositions as an anorectic agent.

BACKGROUND OF THE INVENTION

Hydroxycitric acid (HCA) is found naturally in the rind of Garcinia species of fruit, e.g., *Garcinia cambogia, Garcinia atroviridis* and *Garcinia indica.* Methods known for extracting HCA. from *Garcinia sp.* of fruit are found in Lewis, Y.S., "Methods in Enzymology" (J.M. Lowenstein, Ed., Vol. 13, page 613) (Academic Press, N.Y., 1969) and U.S. Patent No. 5,536,516, the disclosures of which are both incorporated herein by reference as if fully set forth. *Garcinia* rind is also commercially available and tends to comprise 25-35% moisture and 2-5% sodium chloride.

HCA is known to inhibit lipogenesis and act as an appetite suppressant. Many forms of HCA are known and used for encouraging weight loss. U.S. Patent 3,919,254 to Guthrie et al., and related family of U.S. patents, disclose novel ester and amide derivatives of threo-hydroxycitric acid y-lactone and pharmaceutically acceptable salts, for the treatment of obesity and in correcting conditions of lipid abnormalities. U.S. Patent No. 4,312,885, also to Guthrie et al., and related family of U.S. patents, disclose chorocitric acids and their use as anorectic agents for the treatment of obesity in mammals.

U.S. Patent No. 5,656,314, Lo Moffett et al., discloses a salt free HCA extract, in concentrate form, prepared from Garcinia sp. rind, comprising a mixture of 23-54% HCA, in its free form, 6-20% HCA, in its lactone form, and small amounts of citric acid. Food products, such as snack bars and beverages containing salt-free HCA extract are also disclosed.

In order to formulate RCA compositions which are acceptable for oral consumption, there are a number of factors which are important to make them more consumer friendly. One important factor is the sour taste of RCA, which must be eliminated or made negligible. Retaining natural flavor of the *Garcinia* fruit is a factor which increases the composition's desirability as an orally consumed product. It is a preferred factor that the RCA composition be nonhygroscopic so as to facilitate storage and, at the same time, be water soluble so as to enhance the bioavailability of the HCA to the consumer.

With respect to the above-mentioned desired factors, it has been found that the product resulting from direct drying of enriched RCA Garcinia extract retains the desirable flavor of the *Garcinia* fruit and is highly water soluble; however, it is extremely hygroscopic and contains only 25-35% by weight RCA. The pure potassium or sodium salts of RCA are highly water soluble, but they too are extremely hygroscopic and are unable to retain the natural flavor of the *Garcinia* fruit.

CITRIMAX™, a commercially available product(s) containing the calcium salt of RCA, is manufactured by InterHealth Company and is marketed as a herbal mechanism for encouraging weight loss. Reference is made to "The InterHealth Technical Reference Guide for CITRIMAX™" (1994), the contents of which are expressly incorporated herein by reference. In this product, or range of products, RCA is extracted from *Garcinia* sp. and is typically in the stabilized nonlactonized calcium salt of the free form of the acid. In the powder form, such products are non-hygroscopic and essentially water soluble; however, the amount of RCA does not exceed 60% by weight of the product and

the product(s) contain undesirable metals, or potassium. CITRIMAX™ RCA compositions containing pure calcium salts of RCA tend to lose the natural flavors of the *Garcinia sp* fruit and in the liquid form of CITRIMAX™, while being water soluble and containing both free forms and lactone forms of HCA, they tend to be strongly acidic. Furthermore, the liquid forms contain only, at the most, 48% by weight of HCA in the composition.

In view of the foregoing, there is a need in the art for a product which has more than only some of the desired properties for oral consumption and use as a dietary supplement or in a food product. It is therefore an object of the present invention to provide an HCA composition or extract which overcomes the disadvantages of the prior art compositions above, providing an orally acceptable composition which can be easily added to food products, made into dietary supplements and/or which at least provides the public with a useful choice.

SUMMARY OF THE INVENTION

It has been surprisingly found that partial conversion of HCA to its calcium salt results in a form of HCA which has all of the above-mentioned desired properties for oral consumption and use as a dietary supplement and/or in a food product. This partially converted calcium salt form of HCA retains the, natural flavor of the *Garcinia sp* fruit from which it is obtained, is highly water soluble, has minimum hygroscopicity, and can be prepared without the addition of the undesired metals, such as sodium and potassium. Furthermore, it can be advantageously produced as a cream colored free-flowing powder, which makes it not only more suitable for addition to dry food products, but makes it more aesthetically pleasing to the consumer. Previous forms of HCA include tan colored powders, golden viscous liquids and clear solutions.

In addition to achieving the above-mentioned desired properties for oral consumption, the partial calcium salt of HCA results in a composition or extract which contains greater percentages of HCA than have ever before been achieved.

In accordance with a first aspect of the present invention, a hydroxycitric acid (HCA) composition or extract which is potassium-free is provided, and comprises a partial calcium salt of HCA with less than about 2% sodium by weight of the total amount of HCA present in the composition or extract. The amount of HCA present in the composition is up to 65% by weight of the total, and the amount of calcium is between about 8% and about 26% by weight of HCA present in the composition or extract.

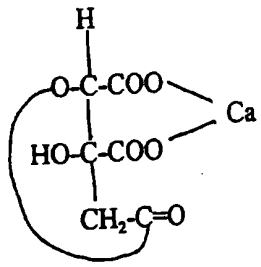
In accordance with a second aspect of the present invention, a dietary supplement or food product is provided which comprises a partial calcium salt of hydroxycitric acid (HCA) in an HCA composition which is potassium-free and which contains less than 2% sodium by weight of HCA present.

As a third aspect of the present invention, a method is provided for preparing a partial calcium salt of hydroxycitric acid (HCA) from a fruit of *Garcinia sp.*, wherein the calcium salt of HCA essentially retains the original flavor of the *Garcinia sp.* fruit from which it is prepared. The partial conversion of HCA to its calcium salt enables a composition or extract which has an increased percentage of HCA, up to 65% by weight of the composition or extract, to be obtained in an extract from *Garcinia sp.* fruit.

As a fourth aspect of the present invention, a method for inhibiting lipogenesis, suppressing appetite and/or promoting weight loss is provided in which a partial calcium salt of hydroxycitric acid (HCA) is produced in a form suitable for oral consumption and orally administering an affective amount of the partial calcium salt of HCA to a patient in need thereof. Other forms of the HCA salt are also contemplated within this aspect of the invention.

DESCRIPTION OF THE PREFERRED EMBODIMENTS

The partial calcium salt of HCA of the present invention has the formula:



Calcium may of course be replaced with other compounds such as potassium or sodium or alkaline earth metals such as magnesium beryllium and barium; however, the inclusion of such other compounds is inconsistent with minimizing dietary intake of such non-desirable compounds. Furthermore, the addition of such compounds compromises the properties of the extract obtained, such as, hygroscopicity, solubility, taste, etc.

It has been found that partial conversion of HCA to its calcium salt not only enables (1) elimination of undesirable materials such as metals and sodium chloride, (2) enriched purity of HCA from *Garcinia sp* fruit, (3) retention of the original taste characteristics of the fruit from which it is obtained and reduction of the sour taste of the acid, but also (4) the ratio of the free form of the HCA to its corresponding y-lactone, present in the *Garcinia sp.* fruit from which it is derived, is maintained.

There are numerous protocols for preparing hydroxycitric acid extracts from *Garcinia sp.* fruit. The commercially available fruit/rind typically contains about 2% to about 5% sodium chloride. It is considered desirable to eliminate as much of the sodium chloride as possible. The amount of HCA present in the commercially available product is typically about 20% by weight. The product also contains about 25% by weight moisture.

The method of preparing an extract from *Garcinia sp* which includes a partial calcium salt of hydroxycitric acid (HCA) generally involves washing the Garcinia rind,

extracting HCA from the rind, producing an insoluble calcium salt of the extracted HCA, partially dissociating the calcium salt and separating out the partial calcium salt of HCA by precipitation or the like.

More specifically, the method for preparing the extract comprises preparing a salt-free solvent extract from the *Garcinia sp.* rind, preferably by hot extraction with acetone and alcohol. The extract is then converted into an insoluble calcium salt of HCA, specifically calcium hydroxy citrate, and removing the components which produce the undesired non-acidic properties, such as color, polyphenolic compounds, sugars and pectins, which will not precipitate, by washing the calcium hydroxycitrate. Next, the calcium hydroxycitrate is partially dissociated by adding dilute sulphuric acid so as to form calcium sulphate and partially converted calcium salt of hydroxycitric acid. The calcium sulphate is then filtered out and the filtrate, enriched HCA solution of partial calcium salt is concentrated to approximately 50% total solids under reduced pressure. The concentrate is then treated with acetone (90%) and alcohol (90%) so as to crystallize the concentrate and form a white crystalline, highly soluble HCA extract.

The above method, which converts HCA to its partial calcium salt, surprisingly enhances the amount of HCA present in the HCA extract, relative to what has been done in the prior art. The composition or extract prepared according to the present invention can contain as much as 65% RCA, by weight of the total composition, preferably the amount is between 55-65% by weight of the total composition.

The amount of calcium is between about 8% and about 26% by 15 weight of the total amount of HCA present in the composition. It has been found that when the amounts of calcium are outside this range the properties desired for oral consumption are not obtainable. For example, below about 8% it has been surprisingly found that the composition obtained has a strong sour taste. Furthermore, when the amount of calcium is below about 8% it is difficult to form a powder. When the amount of calcium exceeds

about 26%, the composition is less soluble. In this regard, reference is made to Example 3 below.

The ratio of the amount of free form of HCA to the amount of lactone form of HCA of the composition obtained according to the present invention is preferably on the order of about 1:0.75. The amount of sodium present in the composition prepared according to the present invention comprises less than about 2% by weight of the total amount of HCA present in the composition. The composition is also essentially potassium-free.

Techniques used to measure the amounts of HCA present in a composition or extract are those well known in the art. Examples of such techniques include high-performance liquid chromatography (HPLC) and gas chromatography mass spectroscopy (GCMS). Such methods can determine the presence of specific acids and amount of each acid present in a sample. Reference in made to The InterHealth Technical Guide For CITRIMAX™ (1994), the Summary of (-)Hydroxycitric Acid Analytical Procedure (The Industrial Laboratories Company) and Kucera, P. *et al.*, "Differential Frontal Analysis of Carboxylic Acids.," Journal of Chromatography, 210 (1981) 373-388.

The composition of the present invention can be produced in any form, for example, liquid or solid; however, it can be advantageously produced in a powder form, preferably as a cream colored free-flowing powder. Powder forms are desirable because free HCA in solution rapidly converts to the lactone form and the lactone form has been shown to be unable to inhibit, or at least to a lesser extent inhibit, ATP-citrate lipase, the enzyme involved in lipogenesis. Previously, it has been difficult to obtain a powder form of HCA extracts, and never before has one been made which contains all of the above-mentioned desired properties for oral consumption.

In a powder form, the HCA composition can be added separately to food products after the food product has been prepared, e.g., sprinkled on top of cereals and the like, or incorporated into the food product during its preparation. Furthermore, due to its high

solubility, the HCA compositions of the present invention can be dissolved in a liquid thereby forming a beverage. Other conventional pharmaceutical forms include, but are not limited to, tablet, capsule, suppository, suspension, emulsion and gel. Furthermore, food products contemplated include, but are not limited to, snack bars, baked goods, beverages and products generally well known in the health and diet industry.

The HCA composition of the present invention may be mixed with conventional organic or inorganic inert pharmaceutical carriers suitable for either oral or parenteral administration, such as water, gelatin, lactose, starch, magnesium stearate and other pharmaceutically acceptable stearates, talc, vegetable oil, gums and the like.

The compositions may be subject to conventional pharmaceutical expedients, such as sterilization and can contain conventional pharmaceutical expedients, such as preservatives, stabilizing agents, emulsifying agents, buffers and the like. Other therapeutically effective compounds may also be added to the compositions of the invention. Such compounds will depend on what the consumer is attempting to accomplish. Examples of such other compounds include, but are not limited to, manganese, vitamin B12, folic acid, vitamin B-6, chromium and vanadium compounds, zinc and other compounds involved in carbohydrate metabolism.

The partial calcium salts of HCA may be used to control energy levels, for assisting in certain metabolic conditions or abnormalities and for modifying appetite, in addition to other uses described above, involving the same biochemical reactions. Athletes may also benefit from extracts containing partial calcium salts of HCA for the positive effects it has on glycogen i.e., promotion of glycogen storage.

Optimal dosages of compositions according to the present invention will be easily determined by a person of skill in the art and will, of course, be based on parameters such as what the desired effect or reason for taking the composition is, for example, larger or smaller doses may be required for different functions, the body weight of the consumer and the form of administration.

Recent clinical trials have shown that 500 milligrams of *Garcinia* extract which contained approximately 250 mg of HCA in addition to 100 micrograms of chromium in a niacin-bound form, taken three times daily, was therapeutically effective.

In the dry form the composition can be added to the food product during preparation of the product.

The term "retaining the original taste of the natural *Garcinia sp.*" means, when an extract prepared in accordance with the present invention is subject to an appropriate taste test, as discussed in Example 1, and compared to the original *Garcinia sp* of fruit from which the extract is derived, the flavors of the original fruit are detectable in the extract.

The term "essentially potassium-free" means that the amounts of potassium are not detectable using known techniques in the art for detecting potassium in HCA extracts.

The term "essentially sodium-free" means less than about 2% sodium is detected, wherein the percentage is by weight of the total amount of HCA present in the extract being tested, using known analytical techniques in the art, for determining the amount of sodium.

The term "enhancing the amounts of HCA present in the composition or extract" means the amounts of HCA present in the HCA composition are increased or greater than compositions previously known in the art. No HCA composition prior to the present invention is known to contain as much as 65% RCA by weight of the total composition.

The method of the present invention will be described in further detail by way of reference to the following examples which are merely exemplary and which are not intended to limit the scope of the invention.

EXAMPLE 1-Method for Preparing a Partially Converted Calcium Salt of HCA:

500 grams of dried *Garcinia* rind raw material is washed with approximately 2 liters of water in a stainless steel vessel. Thereafter, the *Garcinia* rind is extracted with 80% acetone/80% alcohol on a continuous basis with approximately 5 liters of 80% solvent to obtain a salt-free extracted solution. The spent rind is tested for HCA content using known techniques in the art and is typically discarded so as to produce an extracted solution. At this stage the recovery of HCA is of the order 90% ± 5%.

Next, approximately 2kgs of Fuller's earth (a kaolin containing aluminum magnesium silicate) is added to the extracted solution obtained and is mixed for about one hour with continuous agitation at approximately 50 RPM. The mixture is then permitted to settle for a period of about two hours.

Following this, the settled mixture is filtered through a bed of a filter aid in a centrifuge. The filtrate obtained is concentrated by removing the solvent under reduced pressure, approximately 500 grams per meter squared (gms), to approximately 35% total solids containing approximately 24% hydroxycitric acid (HCA) content by weight. The yield at this stage is about 95% of the extracted HCA.

The concentrated extract is again filtered through a bed of a 20 filter aid in a centrifuge to remove any insoluble matter thereby obtaining a filtered extract. Calcium hydroxide (about 65 gms in 350 mls of water) is then added to the filtered extract. This mixture is stirred for approximately 4.0 hours, while maintaining the pH of the solution at about 8.5. The mixture is then filtered through a centrifuge and the filtrate is discarded. The cake obtained is washed continuously with about 10 liters of water until

the filtrate is colorless and no solids are extracted from the filtrate. The yield of HCA at this stage is about 98%.

In the next stage the wet cake of calcium hydroxy citrate obtained is treated with 100 ml of 2M sulphuric acid solution to convert the calcium hydroxycitrate to partial calcium salt of HCA and calcium sulphate. Calcium sulphate is removed by centrifugation and washed in about 500 mls of water. The filtrate is treated with activated carbon (about 250 gms at 75 °C for 2 hours under agitation, cooled and filtered). The filtrate is concentrated to about 225 gms of partial calcium salt of hydroxycitric acid (HCA), the total solids being about 50%. The concentrate is treated with 90% acetone/90% alcohol to obtain pure crystalline, highly soluble partial calcium salt of HCA.

EXAMPLE 2-Analysis of Properties

The properties of a composition or extract according to the present invention, prepared in accordance with the method set forth in Example 1, was characterized and compared to the properties of the known commercially available CITRIMAX™ products prepared by The InterHealth Company. The results are set forth in Table 1 as follows:

TABLE 1

Property	Partial Calcium Salts	CITRIMAX™ REGULAR	CITRIMAX™ HCA 600SXS	CITRIMAX™ LIQUID
Description	Cream color free - flowing powder	Tan colored free-flowing powder	Cream color free-flowing powder	Golden colored clear liquid
Purity of HCA by wt% of extract	55-65%	45-55%	55-60%	40-48%
Calcium by wt % of HCA	8-26%	24-34%	14-26%	Nil
Sodium by wt% of HCA	Nil	8-12%	Nil	Nil
Potassium by wt% HCA	Nil	Nil	24-40%	Nil
Solubility	100%	70%	100%	100%
Natural taste	Present (Moderate acidity)	Nil	Nil	Very Strong acidity
Hygro-scopicity	Nil	Nil	Nil	N/A
Ratio of free form HCA to Lactone	1:0.75	1:0	1:0	0.8:1

Table 1 shows that the extracts in powder form, prepared according to the present invention and containing partial calcium salts, have the highest purity of HCA compared to known CITRIMAX™ extracts/products and are potassium and sodium-free. Further, the extracts of the present invention retain the natural flavor of the original *Garcinia sp.* from which the extract is derived.

The techniques used for analyzing the above products are well known in the art and are referred to below, as follows:

Determination of HCA using HPLC.

Determination of Calcium using atomic absorption spectroscopy.

Determination of Potassium using atomic absorption spectroscopy.

Determination of Sodium using atomic absorption spectroscopy.

Determination of Solubility using the Solubility Test described in USP XXIII.

Determination of Taste was carried out by a panel of 10 people who were (i) given a piece of dried Garcinia rind and (ii) after tasting the rind they were given about 1-5 mg of the Garcinia extract, in powder form, prepared according to the present invention. They were asked whether the rind and the powder tasted the same. They all agreed that the powder had a taste which was substantially similar to the rind.

Determination of Hygroscopicity was carried out by testing the moisture content before and after exposure to the atmosphere for 1 hour, by methods described in USP XXIII.

Determination of Ratio using HPLC.

EXAMPLE 3-Calcium

The effect of the amount of calcium present in the prepared extracts according to the present invention on the properties of the extract, in a powder form, was carried out and the results are presented in Table 2 below.

TABLE 2

Amount of calcium-below 8 wt%	Amount of calcium above 26 wt%
Powder form was difficult to obtain	Increased pH
Highly hygroscopic	Not reported
Strong sour taste	Minimal sour taste
Increased lactone form of HCA	Not reported
Highly soluble	lowered solubility

From the results it can be seen that when the amount of calcium is outside the range of between about 8% and about 26% by weight of the total amount of HCA present in the HCA composition of the present invention, the desired properties of the present invention which make it suitable for oral consumption are not obtainable. The properties of the extracts tested having amounts of calcium below about 8wt% and above about 26 wt%, respectively, were determined, using the same analytical techniques as in Example 2.

What we claim is:

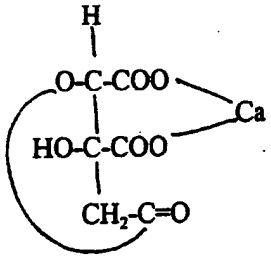
1. A composition comprising a hydroxycitric acid (HCA) partially converted to a calcium salt of the HCA, which composition is essentially potassium-free and which is prepared from an extract of *Garcinia sp.*

2. The composition of claim 1, in the form of. a free-flowing powder.

3. The composition of claim 1, further comprising less than about 2% sodium, by weight of the total amount of HCA present in the composition.

4. The composition of claim 1, further comprising the partial calcium salt in an amount of between about 8% and about 26% by weight of the total amount of HCA present in the composition.

5. The composition of claim 1, wherein the partial calcium salt of HCA has the formula:



6. The composition o1 claim 1, wherein the amount of HCA is between 55-65 % by weight of the total composition.

7. A composition comprising up to 65% hydroxycitric acid (HCA) by weight of the total composition, between about 8% and about 26% calcium, less than about 2%

sodium, said percentages for calcium and sodium being by weight of the total amount of HCA present in the composition and being essentially potassium-free.

8. The composition of claim 7, wherein the HCA is extracted from *Garcinia sp.* of fruit and retains the natural flavors of the original *Garcinia sp.* of fruit from which the HCA is extracted.

9. The composition of claim 7, further comprising a pharmaceutically acceptable carrier or excipient.

10. A dietary supplement comprising a composition as claimed in claim 1.

11. A food product comprising a composition as claimed in claim 1.

12. A method for preparing an hydroxycitric acid (HCA)extract containing a partial calcium salt of HCA comprising the steps of:

extracting HCA from *Garcinia sp.* of fruit by solvent extraction so as to obtain an HCA solvent extract,

removing any non-acidic impurities present in the HCA solvent extract,

converting the extract into an insoluble calcium hydroxycitrate,

partially dissociating the calcium hydroxycitrate to form a partially converted calcium salt of hydroxycitric acid,

separating out the partially converted calcium salt of HCA, and

concentrating the remaining HCA enriched partial calcium salt of HCA solution.

13. The method of claim 12, wherein the amount of HCA present in the concentrated HCA enriched partial calcium salt solution is between 55-65% by weight of the total RCA solution.

14. The method of claim 12, further comprising crystallizing the concentrated RCA solution.

15. A method for inhibiting lipogenesis, promoting weight loss and/or suppressing appetite in an individual comprising: administering an effective amount of a composition of claim 1 to an individual desiring such effects.

16. The method of claim 15, wherein the composition is in a form suitable for oral consumption.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 99/21099

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A23L1/30 A61K31/194 A61K31/365 A23L1/03

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A23L A61K C07C

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	EP 0 866 137 A (LUPIN LAB LTD) 23 September 1998 (1998-09-23)	1-11,15, 16
A	abstract page 2, line 3 -page 5, line 2 examples	12-14
X	EP 0 787 489 A (SIGMA TAU IND FARMACEUTI) 6 August 1997 (1997-08-06)	1-4, 7-11,15, 16
	page 2, line 15 - line 29 page 2, line 54 -page 5, line 18 claims; examples	

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[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

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INTERNATIONAL SEARCH REPORT

International Application No
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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	WO 99 03464 A (RAJU G GANGA ;INTERHEALTH NUTRACEUTICALS INC (US)) 28 January 1999 (1999-01-28)	1,2,4-6, 10-16
A	abstract page 1, line 6 -page 7, line 18 page 10, line 1 -page 12, line 8	7-9
X	US 5 744 161 A (RAJENDRAN RAMASWAMY ET AL) 28 April 1998 (1998-04-28) abstract example 11	1,10
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Form PCT/ISA/210 (continuation of second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 99/21099

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:
   Remark: Although claim(s) 15,16 is(are) directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

2. ☐ Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. ☐ Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest.

☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/US 99/21099

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